



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/533,017

12/12/2005

Maria Cristina Geroni

18086

9303

23389 7590 08/25/2008
SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER

FINN, MEGHAN R

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

08/25/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/533,017 | Applicant(s) GERONI ET AL. | |
| | Examiner MEGHAN FINN | Art Unit 1614 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,5,7 and 11-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,7 and 11-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's addition of "to those patients whose CYP3A levels indicate formation of a metabolite of nemorubicin more active than nemorubicin" is new matter. Applicants assert that this is taught in the specification at page 2, lines 9-15, however the specification teaches that there is a metabolite of nemorubicin which is more cytotoxic than nemorubicin, when broken down in the liver, however it does not say anything about CYP3A being the enzyme, or that explain how the CYP3A levels would indicate the presence of this more active metabolite. This new addition presents a new idea which wasn't presented in the original application and is thus new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, 7, and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (Cytochrome P-450...) in view of Beulz-Riché et al. (Effects of paclitaxel...), each already of record in pages 2-5 of the previous action mailed December 05, 2007, of which reasons are herein incorporated by reference, in further view of Pacciarini et al. (WO 00/15203).

Art Unit: 1614

Applicant has amended the claims such that all claims are for a method of treating a patient suffering from liver cancer or liver metastases. As discussed previously, Collins et al. teach using ERMBT as a way to individualize doses of an anticancer drug docetaxel, which is metabolized by CYP3A. (page 1203, first paragraph). They do not teach nemorubicin, however Beulz-Riché et al. teach that nemorubicin(also known as MMDx or methoxymorpholinodoxorubicin) is metabolized by CYP3A (abstract). Neither mention treatment of liver cancer, however Pacciarini et al. teach that methoxymorpholino doxorubicin (nemorubicin) is useful for treatment of liver cancer (abstract). They further teach that the compound is more potent when administered in vivo, and that the cytotoxic activity of MMDX is increased in the presence of liver microsomes, suggesting that MMDX may be transformed into highly cytotoxic metabolites (page 2, lines 6-14). As it was known in the art at the time of the invention that MMDX treats liver cancer, and that it is a metabolite of MMDX that is potentially much more active, it would have been obvious to one of ordinary skill in the art at the time of the invention to use MMDX to treat liver cancer, and to try to determine the optimum dosage, especially of the more cytotoxic metabolite. As MMDX is known in the art to be metabolized by CYP3A, there would have been an obvious desire to determine the amount of MMDX being metabolized.

Collins et al. teaches a standard test, ERMBT, and that is can be used to individualize dosages of an anti-cancer drug. Despite the fact that Collins et al. is using the test to determine those that cannot tolerate docetaxel, one of ordinary skill in the art at the time of the invention would recognized that the test will also indicate who can

Art Unit: 1614

tolerate the drug, and that it could be used on another drug which CYP3A metabolizes. It would have been obvious to use this test on MMDX to determine the amount metabolized in order to individualize dosages for liver cancer treatment. There is an obvious motivation, as optimization of dosages for anti-cancer drugs is a very common treatment, and furthermore, as taught by Collins et al. drugs which are metabolized by CYP3A are excellent candidates for individualization of dosages because CYP3A is known to have large inter-individual variability (page 1203, first paragraph). It would have been obvious to one of ordinary skill in the art at the time of the invention that dosages of MMDX could be individualized, due to being metabolized by CYP3A, and that a known test for another drug metabolized by CYP3A could be used to determine the amount metabolized. Thus claims 1, 3, 5, 7, and 11-14 are unpatentable over Collins et al. in view of Beulz-Riché et al. in further view of Pacciarini et al.

Response to arguments

Applicant has argued that the teachings of Collins et al. are misplaced. That Collins et al. only teaches that ERBMT is an excellent test to determine docetaxel metabolism, and that this test is used to shield patients who would metabolize docetaxel too rapidly. The examiner does not disagree that Collins et al. teaches they above, but they also teach that docetaxel is metabolized by CYP3A and that it is an excellent candidate for dosage individualization because of this metabolism by CYP3A. This would lead one of ordinary skill in the art to believe that ERBMT could be used to

Art Unit: 1614

determine optimum individualized dosages for other drugs also metabolized by ERBMT. Furthermore, in identifying patients for which docetaxel would not be good, they are also identifying patients for which docetaxel would be useful, and thus applicant's arguments that the teaching of shielding patients rather than treating them is not persuasive.

The prior art already identifies that nemorubicin (MMDX) is useful for treatment of liver cancer, and that there is a metabolite that is more active than MMDX. Both the method of Collins et al. and the instant invention use the concept of metabolism of a drug by CYP3A to determine whether the drug would be useful for the individual patient or not, and it would have been obvious to substitute MMDX for docetaxel as it is another drug also known to be metabolized by CYP3A.

Applicant has also argued in the supplemental remarks that the finding of the present invention is that that CYP3A4 isoenzyme converts nemorubicin into a more active metabolite. This is however, not taught the original specification, as discussed above. All applicant has stated in the specification is that nemorubicin is known to be metabolized into more cytotoxic metabolites in the presence of liver microsomes, this is taught by Pacciarini et al. and thus is not a novel finding of this invention. Furthermore, CYP3A is known to be the primary metabolizer of nemorubicin, and thus it would have been obvious to use the test for CYP3A metabolization, as taught by Collins et al., in order to determine the amount of nemorubicin metabolized.

Conclusion

No claims are allowed.

Art Unit: 1614

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 7:30am-5pm Mon-Thu, 7:30am-4pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614